January 8, 1999

This document was submitted to EPA by a registrant in connection with EPA's evaluation of this chemical, and it is presented here exactly as submitted.

February 18, 1998

Mr. Tom Moriarity
Chemical Review Manager- ODM
Special Review and Reregistration Division (H7508W)
Office of Pesticide Programs
U.S. Environmental Protection Agency
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. Moriarity:

Gowan Company submitted a document entitled "Registrants Response to the USEPA Hazard Identification Report for Oxydemeton-Methyl" on January 6, 1998. The USEPA (telecon, J. Rowland to V. Piccirillo, February 9, 1998) requested that additional information be submitted to supplement this document. This information included submission of a draft report from the recently completed 7-day dermal toxicity study in rats and a rationale explaining Gowan's technical concerns related to the previously submitted 14-day dermal toxicity study in rats. The Agency recently requested that Gowan also submit a copy of the previously submitted final report from the "Percutaneous Absorption of METASYSTOX-R in the Rhesus Monkey" (telecon, T. Moriarity to B.Codrea, February 17, 1998).

Attached to this letter is a document which addresses Gowan's technical concerns related to the previous 14-day study. I have also enclosed a copy of an Unaudited Summary Report from "A 7-Day Dermal study of the Cholinesterase-Inhibiting Potential of Oxydemeton-methyl (Metasystox-R) in Rats" as well as a copy of the final report from the "Percutaneous Absorption of METASYSTOX-R in the Rhesus Monkey".

Should you have any questions or require additional information, please feel free to contact Ms. Codrea (520-819-1543) or myself.

Sincerely yours,

Vincent J. Piccirillo, Ph.D., DABT
Consulting Toxicologist

cc. Elizabeth Codrea, Gowan Company
Jes Rowland, USEPA/HED

TECHNICAL CONCERNS RELATED TO MRID 40499304
"Fourteen-Day Cholinesterase Activity Study of Oxydemeton-Methyl
(METASYSTOX-R) with Rats by Dermal Application"

The EPA HAZID committee recommended using the "Fourteen-Day Cholinesterase Activity Study of Oxydemeton-Methyl (METASYSTOX-R) with Rats by Dermal Application" as the critical study for the short-term occupational or residential exposure risk assessment of ODM. Because of some technical concerns related to that study, Gowan Company proceeded with a new 7-day dermal toxicity study in rats. The technical concerns related to the previous study can be summarized as follows:

1. A great deal of debate has occurred over the last several years regarding the appropriate sampling procedures and analytical methods that should be used for cholinesterase determinations. In review of any cholinesterase data, it is important to assure that the laboratory performed the determinations using appropriate and validated methods. The above captioned report stated that a modified Ellman method was used. The report specified that the chromogen was 6,6-dithiodinicotinic acid, however, the standard Ellman method uses dithiobisnitrobenzoic acid (DNTB) as the chromogen. The acceptability and validity of using a chromogen other than DNTB is uncertain.

2. Information critical to validating the assay such as temperature, method of sampling handling during the assay, volume of assay material, buffers used and wavelength were not included in the report. Variations in these parameters may seriously impact the cholinesterase results.

3. Review of the mean brain cholinesterase results and statistical analysis suggested that brain ChE was inhibited at dose levels below those causing plasma or RBC ChE inhibition. A careful evaluation of the individual data showed that this anomaly was likely an artifact of evaluating small numbers of animals at each dose level. The individual results also indicated the brain cholinesterase values for 2 of the 5 control females were exceedingly high when compared to the other controls in this study as well as the controls from the concurrent gavage and dietary studies. The majority of the control cholinesterase values were in the 13-14 range where the values for these two control females were 16.1 and 17.8 severely skewing the study results.

Because of the methodological uncertainties and the apparent statistical anomaly, Gowan Company conducted the new 7-day study using contemporaneous methodologies for cholinesterase determinations and increased the animal population to 10 males and 10 females per group.